DETAILED ACTION

Amendment Entry

1. Applicant's amendment and response filed April 1, 2011, is acknowledged and has been entered. Claim 3 has been amended. Claim 9 has been cancelled. Accordingly, claims 1, 3 5-8, and 10 are pending and are under examination.

Claim Rejections / Objections

2. All rejections or objections not reiterated herein have been withdrawn.

3. The rejections of claim 9 are now moot in light of Applicant's cancellation of the claim.

4. In light of Applicant's amendment and arguments, the rejection of claims 1, 3, 5, 7, 8, and 10 under 35 U.S.C. 112, second paragraph, is hereby, withdrawn.

5. In light of Applicant's amendment and arguments, the rejection of claims 1, 3,5-8, and 10 under 35 U.S.C. 102(a) as being anticipated by Scheiflinger et al. (US 2004/0214346 A1), is hereby, withdrawn.

6. In light of Applicant's amendment and arguments, the rejection of claims 1, 3, 7, 8, and 10 under 35 U.S.C. 102(a) as being inherently anticipated by Konetschny et al. (Development of a Highly Sensitive and Specific Enzyme-linked Immunosorbent Assay for the Detection of ADAMTS-13 in Human Plasma, Blood 102 (11) Abstract #4062 (November 16, 2003)) in light of Scheiflinger et al. (US 2004/0214346 A1), is hereby, withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Konetschny et al. (Development of a Highly Sensitive and Specific Enzyme-linked Immunosorbent Assay for the Detection of ADAMTS-13 in Human Plasma, Blood 102 (11) Abstract #4062 (November 16, 2003)) in view of Scheiflinger et al. (US 2004/0214346 A1).

Konetschny et al. teach detecting and analyzing thrombosis, i.e. thrombophilia, using antibodies (anti-vWFcp or anti-ADAMTS-13) that specifically bind to von Willebrand factor (vWF) cleaving protease or ADAMTS-13 in human plasma sample in

an enzyme-linked immunosorbent assay (ELISA) as detection method (1st full paragraph). Capture anti-vWFcp (anti-ADAMTS-13) polyclonal antibody is coated onto microtiter plate to capture vWFcp and detection anti-vWFcp MAb (242/H2) is conjugated to alkaline phosphatase so as to provide binding, detection, and measurement of vWFcp antigen present in the plasma (2nd full paragraph). Konetschny et al. show that a decrease in concentration of vWFcp manifested as a deficiency in ADAMTS-13 in a patient in comparison to healthy control subject provides indication of occurrence of thrombosis (1st and 3rd full paragraphs).

Konetschny et al. differ from the instant invention in failing to teach a kit.

Scheiflinger et al. disclose a kit having antibodies, solid phase, label, and reagents for use in immunological assay method.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the anti-ADAMTS-13 antibodies and reagents taught by Konetschny into a kit format as taught by Scheiflinger because kit formats are conventional and well-known for their recognized advantages of convenience and economy.

Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1, 3 5, 7, 8, and 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for determining severity of thrombophilia in patients having pulmonary embolism, cerebral infarction, veno-occlusive disease (VOD), and deep vein thrombosis (DVT) by measuring for von WIllebrand factor-cleaving protease (vWFcp) in blood using MAb WH10, MAb WH63.1, and WH2-22.1A in a sandwich immunoassay to bind and react to vWFcp and correlated with the vWFcp levels in normal subjects having no disease using the same monoclonal antibodies in a sandwich immunoassay, does not reasonably provide enablement for determining severity of thrombophilia in any and all thrombosis patients using any other combination of antibodies that may bind to vWFcp. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

As set forth in In re Wands, 858 F .2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The nature of the invention- the invention is directed to a method of determining severity of thrombophilia using MAb WH10, MAb WH63.1, and WH2-22.1A in a

sandwich immunoassay to bind and react to vWFcp to measure vWFcp in patients having pulmonary embolism, cerebral infarction, veno-occlusive disease (VOD), and deep vein thrombosis (DVT) and correlating the result with vWFcp levels in normal subjects having no such disease.

The state of the prior art- Konetschny et al. (Blood 102 (11) Abstract #4062 (November 16, 2003)) show a nexus between thrombosis and vWFcp. Konetschny et al. specifically teach a capture anti-vWFcp (anti-ADAMTS-13) polyclonal antibody and detection MAb 242/H2 to detect and measure vWFcp in the plasma of thrombotic patients; and show that a decrease in vWFcp in comparison to healthy control subject provides indication of occurrence of thrombosis (1st and 3rd full paragraphs).

The predictability or lack thereof in the art- there is no predictability based on the instant specification that any anti-vWFcp antibodies exclusive of MAb WH10, MAb WH63.1, and WH2-22.1A which have been generated, tested, and immunoassayed in Applicant's disclosure in a sandwich assay, can provide a reactive and diagnostic determination of severity of thrombophilia in patients having pulmonary embolism, cerebral infarction, VOD, and DVT, as encompassed by the claimed invention.

The amount of direction or guidance present- appropriate guidance is provided by the specification for the claimed method to work using MAb WH10, MAb WH63.1, and WH2-22.1A combined as capture and detection antibodies in a sandwich immunoassay.

The presence or absence of working examples- there are no working examples that show any other vWFcp antibodies that bind and react to vWFcp and provide correlative determination of severity of thrombophilia. There are no working examples that show diagnostic determination of severity of thrombophilia in patients having pulmonary embolism, cerebral infarction, VOD, and DVT using any and all antibodies that may bind to vWFcp, which is encompassed by the claims.

The quantity of experimentation necessary- it would require undue amount of experimentation for the skilled artisan to make and use the method as claimed.

The breadth of the claims- as recited, the instant claims are directed to determining severity of thrombophilia in subjects having pulmonary embolism, cerebral infarction, VOD, and DVT using any other antibodies, including those taught by Konetschny; without stating how this can be done without undue experimentation.

The Abstract and paragraphs [0009, 0023, 0025, 0030-0033] of Applicant's disclosure provide that severity or degree of thrombophilia in patients experiencing thrombosis has been shown to be detected and determined using a combination of monoclonal antibodies including MAb WH10, MAb WH63.1, and WH2-22.1A in a sandwich immunoassay. Example 1, Table 1, and [0054] show using the combination of the monoclonal antibodies to measure vWFcp, specifically using WH10 as capture antibody and WH63.1, WH2-22-1A, or Applicant's anti-vWFcp polyclonal antibody as detection antibody in a sandwich immunoassay in patients manifesting thrombosis occurring with pulmonary embolism, cerebral infarction, VOD, and DVT. Applicant

found and showed that the average concentrations of vWFcp in the patient groups show significantly lowered levels. See also Figure 2 (capture MAb WH10 and detection WH2-22.1A1), Figure 3 (capture MAb WH10 and detection MAb WH63.10, and Figure 4 (capture MAb WH10 and Applicant's detection PoAb).

While the specification shows that the combination of the antibodies aforementioned provide a correlation with the severity of thrombophilia in patients suffering thrombosis from disease including pulmonary embolism, cerebral infarction, VOD, and DVT, the specification does not show or exemplify working examples which enable use of any other combination of anti-vWFcp antibodies, which appears to be encompassed in the claimed invention. The fact that the method appears to work using MAb WH10, MAb WH63.1, and WH2-22.1A in a sandwich immunoassay to provide a determination of severity of thrombophilia in patients suffering from thrombosis in selected groups of patients is not sufficient to enable the breadth of the claimed method using any anti-vWFcp antibodies. The specification also does not establish a direct correlation between the disclosed antibodies and all other anti-vWFcp antibodies, including those taught by Konetschny, which would lead the skilled artisan to say that if the claimed method works for MAb WH10, MAb WH63.1, and WH2-22.1A in a sandwich immunoassay then it should also work with other known anti-vWFcp antibodies, including those taught by Konetschny, to enable the breadth of the claimed invention. While it is not necessary to show working examples for every possible embodiment, there should be sufficient teaching in the specification that would suggest to the skilled

artisan that the breadth of the claimed method is enabled. This is not the case in the instant specification.

According to Strongin (Sensitivity, Specificity, and Predictive Value of Diagnostic Tests: Definitions and Clinical Applications, Laboratory Diagnosis of Viral Infections, Lennette, E. ed., Marcel Dekker Inc., New York, pages 211-219 (1993)), a number of characteristics need to be considered in the development of any suitable diagnostic assay. These characteristics include the following: 1) sensitivity of the assay, 2) true-positive test rate, 3) false-negative test rate, 4) specificity, 5) false-positive test rate, 6) true-negative test rate, 7) predictive value, 8) prevalence, 9) efficiency, and 10) accuracy of the diagnostic assay. Additional considerations are also examined to enable the clinician to practice the invention including specific assessment of 1) maximum sensitivity desired, 2) maximum specificity desired, 3) maximum efficiency desired, 4) how sensitivity or specificity is maximized, and 5) how predictive value is maximized. An essential understanding of these factors is required to enable a skilled artisan to accurately use and interpret any given diagnostic test. Since the specification lacks any teaching of how the diagnostic tests were performed using other monoclonal antibodies other than those generated by Applicant supra, including information regarding the patients from which the samples were obtained, and whether any consideration was given to the characteristics aforementioned, it would require undue consideration for one skilled in the art to make and use the invention as claimed.

Patent protection is granted in return for enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v.

Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1996), stating in context of the utility requirement that "a patent is not a hunting license. It is not a reward for the search, but for compensation for its successful conclusion." Tossing out the mere germ of an idea does not constitute an enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by the inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. Genentech Inc. v. Novo Nordisk A/A (CAFC) 42 USPQ2d 1001. That requirement has not been met in the instant disclosure. Therefore, it is deemed that one of ordinary skill in the art could not make and use the invention as claimed without undue experimentation.

Response to Arguments

9. Applicant's arguments with respect to claims 1, 3, 5-8, and 10 have been considered but are moot in view of the new grounds of rejection.

10. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GAILENE R. GABEL whose telephone number is (571)272-0820. The examiner can normally be reached on Monday, Tuesday, Thursday, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark L. Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/GAILENE R. GABEL/
Primary Examiner, Art Unit 1641

June 15, 2011